

# PATENT COOPERATION TREATY

PCT



From the INTERNATIONAL BUREAU

## NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

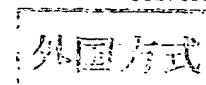
AOYAMA, Tamotsu  
Aoyama & Partners  
IMP Building  
3-7, Shiromi 1-chome  
Chuo-ku, Osaka-shi  
Osaka 540-0001  
JAPON

Date of mailing (day/month/year) 18 August 1999 (18.08.99)	
Applicant's or agent's file reference 661101	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP99/03242	International filing date (day/month/year) 18 June 1999 (18.06.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 26 June 1998 (26.06.98)
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
26 June 1998 (26.06.98)	10/180008	JP	06 Augu 1999 (06.08.99)

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p>Authorized officer Juan Cruz</p> <p>Telephone No. (41-22) 338.83.38</p>
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# PATENT COOPERATION TREATY

PCT



From the INTERNATIONAL BUREAU

## NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

AOYAMA, Tamotsu  
Aoyama & Partners  
IMP Building  
3-7, Shiromi 1-chome  
Chuo-ku, Osaka-shi  
Osaka 540-0001  
JAPON

Date of mailing (day/month/year) 06 January 2000 (06.01.00)		IMPORTANT NOTICE	
Applicant's or agent's file reference 661101			
International application No. PCT/JP99/03242	International filing date (day/month/year) 18 June 1999 (18.06.99)	Priority date (day/month/year) 26 June 1998 (26.06.98)	
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,EP,JP,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
CA,MX

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 06 January 2000 (06.01.00) under No. WO 00/00506

### REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

### REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer J. Zahra Telephone No. (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF RECEIPT OF  
RECORD COPY

(PCT Rule 24.2(a))



To:

AOYAMA, Tamotsu  
Aoyama & Partners  
IMP Building  
3-7, Shiromi 1-chome  
Chuo-ku, Osaka-shi  
Osaka 540-0001  
JAPON

Date of mailing (day/month/year) 13 July 1999 (13.07.99)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 661101	International application No. PCT/JP99/03242

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

SAGAMI CHEMICAL RESEARCH CENTER et al (for all designated States except US)  
KATO, Seishi et al (for US)

International filing date : 18 June 1999 (18.06.99)  
Priority date(s) claimed : 26 June 1998 (26.06.98)  
Date of receipt of the record copy  
by the International Bureau : 02 July 1999 (02.07.99)  
List of designated Offices :

EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
National : AU, CA, JP, MX, US

## ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- ☒ time limits for entry into the national phase  
☒ confirmation of precautionary designations  
☒ requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer: Y. KUWAHARA Telephone No. (41-22) 338.83.38
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1/4

661101

## PCT REQUEST

Original (for SUBMISSION) - printed on 17.06.1999 05:52:05 PM

0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request Prepared using	PCT-EASY Version 2.84 (updated 01.06.1999)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	Japanese Patent Office (RO/JP)
0-7	Applicant's or agent's file reference	661101
I	Title of invention	HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS
II	Applicant	
II-1	This person is:	applicant only
II-2	Applicant for	all designated States except US
II-4	Name	SAGAMI CHEMICAL RESEARCH CENTER
II-5	Address:	4-1, Nishi-Ohnuma 4-chome, Sagamihara-shi, Kanagawa 229-0012 Japan
II-6	State of nationality	JP
II-7	State of residence	JP
II-8	Telephone No.	(0427) 42-4692
II-9	Facsimile No.	(0427) 66-2846
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant only
III-1-2	Applicant for	all designated States except US
III-1-4	Name	PROTEGENE INC.
III-1-5	Address:	2-20-3, Naka-cho, Meguro-ku, Tokyo 153-0065 Japan
III-1-6	State of nationality	JP
III-1-7	State of residence	JP

## PCT REQUEST

661101

Original (for SUBMISSION) - printed on 17.06.1999 05:52:05 PM

<b>III-2</b>	<b>Applicant and/or inventor</b>	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	KATO, Seishi
III-2-5	Address:	3-46-50, Wakamatsu, Sagamihara-shi, Kanagawa 229-0014 Japan
III-2-6	State of nationality	JP
III-2-7	State of residence	JP
<b>III-3</b>	<b>Applicant and/or inventor</b>	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	KIMURA, Tomoko
III-3-5	Address:	302, 4-1-28, Nishiikuta, Tama-ku, Kawasaki-shi, Kanagawa 214-0037 Japan
III-3-6	State of nationality	JP
III-3-7	State of residence	JP
<b>IV-1</b>	<b>Agent or common representative; or address for correspondence</b>	
	The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name (LAST, First)	AOYAMA, Tamotsu
IV-1-2	Address:	AOYAMA & PARTNERS IMP Building, 3-7, Shiromi 1-chome, chuo-ku, Osaka-shi, Osaka 540-0001 Japan
IV-1-3	Telephone No.	(06) 6949-1261
IV-1-4	Facsimile No.	(06) 6949-0361
<b>IV-2</b>	<b>Additional agent(s)</b>	
		additional agent(s) with same address as first named agent
IV-2-1	Name(s)	TAMURA, Yasuo; IWASAKI, Mitsutaka
<b>V</b>	<b>Designation of States</b>	
<b>V-1</b>	<b>Regional Patent</b> (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT
<b>V-2</b>	<b>National Patent</b> (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AU CA JP MX US

## PCT REQUEST

661101

Original (for SUBMISSION) - printed on 17.06.1999 05:52:05 PM

<b>V-5</b>	<b>Precautionary Designation Statement</b> In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
<b>V-6</b>	<b>Exclusion(s) from precautionary designations</b>	NONE
<b>VI-1</b>	<b>Priority claim of earlier national application</b>	
VI-1-1	Filing date	26 June 1998 (26.06.1998)
VI-1-2	Number	Patent Application No. 10-180008
VI-1-3	Country	JP
<b>VI-2</b>	<b>Priority document request</b> The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1
<b>VII-1</b>	<b>International Searching Authority Chosen</b>	European Patent Office (EPO) (ISA/EP)
<b>VIII</b>	<b>Check list</b>	number of sheets      electronic file(s) attached
VIII-1	Request	4      -
VIII-2	Description (excluding sequence listing part)	59      -
VIII-3	Claims	1      -
VIII-4	Abstract	1      661101.txt
VIII-5	Drawings	10      -
VIII-6	Sequence listing part of description	45      -
VIII-7	TOTAL	120
	<b>Accompanying items</b>	paper document(s) attached      electronic file(s) attached
VIII-8	Fee calculation sheet	✓      -
VIII-15	Nucleotide and/or amino acid sequence listing in computer readable form	separate diskette
VIII-16	PCT-EASY diskette	-      diskette
VIII-17	Other (specified):	Revenue stamps of transmittal fee for receiving office      -
VIII-17	Other (specified):	Request for transmittal of priority document      -
<b>VIII-18</b>	<b>Figure of the drawings which should accompany the abstract</b>	
<b>VIII-19</b>	<b>Language of filing of the international application</b>	English

## PCT REQUEST

661101

Original (for SUBMISSION) - printed on 17.06.1999 05:52:05 PM

IX-1	Signature of applicant or agent	
IX-1-1	Name (LAST, First)	AOYAMA, Tamotsu

## FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	
10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

## FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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REC'D 04 OCT 2000

WIPO

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 661101	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP99/03242	International filing date (day/month/year) 18/06/1999	Priority date (day/month/year) 26/06/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  12/01/2000	Date of completion of this report  29.09.2000
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Celler, J  Telephone No. +49 89 2399 7336





# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP99/03242

## I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

### Description, pages:

1-59 as originally filed

### Claims, No.:

1-6 as originally filed

### Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**see separate sheet**

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1 - 6 (partly).

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP99/03242

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
  
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  
- ☒ no international search report has been established for the said claims Nos. 1 - 6 (partly).

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims 1 - 6 (partly)
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1 - 6 (partly)
Industrial applicability (IA)	Yes:	Claims 1 - 6 (partly)
	No:	Claims

### 2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP99/03242

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**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**se separate sheet**

**Re Item I**

**Basis of the report**

The present International Preliminary Examination Report is also based on pages 1 - 45 of the provided sequence listing.

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The present application relates to proteins characterised by the presence of hydrophobic regions, DNAs coding for these proteins, corresponding expression vectors and cells capable of expressing the coding DNAs.

Due to lack of unity of the invention, the international search report has been established only in regard to the sequences shown in the sequence listing as SEQ ID No. 1, 11 and 21. The present opinion on novelty, inventive step and industrial applicability of the invention is given only in regard to these sequences.

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following document:

D1: WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998

2. As none of the documents constituting prior art in the sense of Rule 64(1)(b) PCT that are identified in the International Search Report, discloses a sequence

identical to any of sequences with SEQ ID NO.: 1, 11 or 21 of the present application, the examined subject matter of Claims 1 - 6 is regarded as novel in the sense of Art 33(2) PCT.

3. For the purpose of evaluating the inventive step of the present application D1 was chosen as the closest prior art document. D1 describes cloning of cDNA fragments from a cDNA library. The sequences of the cDNA clones were subsequently examined for the presence of open reading frames (ORF). The hydrophobicity/hydrophilicity profiles were obtained by the method of Kyte-Doolittle for the ORFs and the protein sequences comprising hydrophobic regions were so identified (p. 16, line 27, ff.; p. 18, line 9, ff.). Subsequently, the full length cDNAs with ORFs displaying hydrophobic regions were obtained and used to construct expression vectors and to generate the corresponding proteins by transfection of COS7 cells (p. 19, line 11 - p. 21 line 15).

Therefore, a skilled person faced with the problem of provision of further proteins characterised by the presence of hydrophobic regions, the corresponding DNA, expression vectors and expressing cells would use the approach of D1. The skilled person would also have the possibility to introduce a large number of modifications, which are well known in the art. For example, it would have no bearing on the inventive step whether to establish the presence of a hydrophobic region based on a full length of cDNA or just a fragment thereof. Similarly, expression of chimeric fusions of proteins or fragments thereof is equally well established in the art as expression of full length proteins in non-tagged form.

Thus, provision of further proteins comprising hydrophobic regions could be considered inventive only if the newly identified proteins were associated with an unexpected technical effect. As the mere presence of the hydrophobic region per se does not lead to any unexpected or advantageous effect and no further evidence for such an effect is given in the present application and because the protein provision was accomplished by methods well known in the art, no inventive step can be acknowledged for Claims 1 - 6 (Art. 33(3) PCT).

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/JP99/03242

**Re Item VI**

**Certain documents cited**

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99/57270	11.11.99	28.04.99	01.05.98

Said document has been published and filed after the claimed priority date of present application. It does therefore not constitute prior art in the sense of Rule 64(1)(b) PCT. It will, however, become of relevance for novelty of claimed subject matter during the regional phase of examination (see for example SEQ ID 12 of WO 99/57270).

**Re Item VIII**


**Certain observations on the international application**

The term "a transformation eucariotic cell" renders Claim 6 obscure, because it is impossible to decide whether it relates to a process (a transfection of a eukaryotic cell) or to a product (a transfected eukaryotic cell) (Art. 6 PCT). It should also be noted that especially in relation to cells of higher-eukaryotic origin the term "transformation" or "transformed" is preferably used to describe the acquisition of a new phenotype, for example the ability of tumor formation. To describe the introduction of DNA constructs into cells of higher-eukaryotic origin the term "transfection" is generally accepted in the art. According to the requirements of Rule 10(e) PCT, terms should be used in the way that is generally accepted in the art.

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 661101	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP99/03242	International filing date (day/month/year) 18/06/1999	Priority date (day/month/year) 26/06/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input checked="" type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand  12/01/2000	Date of completion of this report  29.09.2000	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Celler, J  Telephone No. +49 89 2399 7336	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP99/03242

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-59 as originally filed

**Claims, No.:**

1-6 as originally filed

**Drawings, sheets:**

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 1 - 6 (partly).



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP99/03242

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
  
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  
- ☒ no international search report has been established for the said claims Nos. 1 - 6 (partly).

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims 1 - 6 (partly)
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1 - 6 (partly)
Industrial applicability (IA)	Yes:	Claims 1 - 6 (partly)
	No:	Claims

### 2. Citations and explanations

**s e separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP99/03242

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**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**s separate sheet**

**Re Item I**

**Basis of the report**

The present International Preliminary Examination Report is also based on pages 1 - 45 of the provided sequence listing.

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The present application relates to proteins characterised by the presence of hydrophobic regions, DNAs coding for these proteins, corresponding expression vectors and cells capable of expressing the coding DNAs.

Due to lack of unity of the invention, the international search report has been established only in regard to the sequences shown in the sequence listing as SEQ ID No. 1, 11 and 21. The present opinion on novelty, inventive step and industrial applicability of the invention is given only in regard to these sequences.

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following document:

D1: WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998

2. As none of the documents constituting prior art in the sense of Rule 64(1)(b) PCT that are identified in the International Search Report, discloses a sequence

identical to any of sequences with SEQ ID NO.: 1, 11 or 21 of the present application, the examined subject matter of Claims 1 - 6 is regarded as novel in the sense of Art 33(2) PCT.

3. For the purpose of evaluating the inventive step of the present application D1 was chosen as the closest prior art document. D1 describes cloning of cDNA fragments from a cDNA library. The sequences of the cDNA clones were subsequently examined for the presence of open reading frames (ORF). The hydrophobicity/hydrophilicity profiles were obtained by the method of Kyte-Doolittle for the ORFs and the protein sequences comprising hydrophobic regions were so identified (p. 16, line 27, ff.; p. 18, line 9, ff.). Subsequently, the full length cDNAs with ORFs displaying hydrophobic regions were obtained and used to construct expression vectors and to generate the corresponding proteins by transfection of COS7 cells (p. 19, line 11 - p. 21 line 15).

Therefore, a skilled person faced with the problem of provision of further proteins characterised by the presence of hydrophobic regions, the corresponding DNA, expression vectors and expressing cells would use the approach of D1. The skilled person would also have the possibility to introduce a large number of modifications, which are well known in the art. For example, it would have no bearing on the inventive step whether to establish the presence of a hydrophobic region based on a full length of cDNA or just a fragment thereof. Similarly, expression of chimeric fusions of proteins or fragments thereof is equally well established in the art as expression of full length proteins in non-tagged form.

Thus, provision of further proteins comprising hydrophobic regions could be considered inventive only if the newly identified proteins were associated with an unexpected technical effect. As the mere presence of the hydrophobic region per se does not lead to any unexpected or advantageous effect and no further evidence for such an effect is given in the present application and because the protein provision was accomplished by methods well known in the art, no inventive step can be acknowledged for Claims 1 - 6 (Art. 33(3) PCT).

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/JP99/03242

**Re Item VI**

**Certain documents cited**

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99/57270	11.11.99	28.04.99	01.05.98

Said document has been published and filed after the claimed priority date of present application. It does therefore not constitute prior art in the sense of Rule 64(1)(b) PCT. It will, however, become of relevance for novelty of claimed subject matter during the regional phase of examination (see for example SEQ ID 12 of WO 99/57270).

**Re Item VIII**

**Certain observations on the international application**

The term "a transformation eucariotic cell" renders Claim 6 obscure, because it is impossible to decide whether it relates to a process (a transfection of a eukaryotic cell) or to a product (a transfected eukaryotic cell) (Art. 6 PCT). It should also be noted that especially in relation to cells of higher-eukaryotic origin the term "transformation" or "transformed" is preferably used to describe the acquisition of a new phenotype, for example the ability of tumor formation. To describe the introduction of DNA constructs into cells of higher-eukaryotic origin the term "transfection" is generally accepted in the art. According to the requirements of Rule 10(e) PCT, terms should be used in the way that is generally accepted in the art.

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>661101</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/JP 99/ 03242</b>	International filing date (day/month/year) <b>18/06/1999</b>	(Earliest) Priority Date (day/month/year) <b>26/06/1998</b>
Applicant <b>SAGAMI CHEMICAL RESEARCH CENTER et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☐

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒

contained in the international application in written form.

☒

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority in written form.

☐

furnished subsequently to this Authority in computer readable form.

☐

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

**4. With regard to the title,**☒

the text is approved as submitted by the applicant.

☐

the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**☒

the text is approved as submitted by the applicant.

☐

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. The figure of the drawings to be published with the abstract is Figure No.**☐

as suggested by the applicant.

☐

because the applicant failed to suggest a figure.

☐

because this figure better characterizes the invention.

☒

None of the figures.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/JP 99/03242**B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-6 (partially), see additional sheet, subject 1.

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

1. Claims: 1-6 partially

A protein comprising the amino acid sequence SEQ ID NO 1, a DNA SEQ ID NO 11 or 21, encoding this protein, as well as an expression vector capable of expressing this sequence and a eukaryotic cell expressing the DNA

2. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 2 and DNA SEQ ID 12 and 23

3. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 3 and DNA SEQ ID 13 and 25

4. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 4 and DNA SEQ ID 14 and 27

5. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 5 and DNA SEQ ID 15 and 29

6. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 6 and DNA SEQ ID 16 and 31

7. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 7 and DNA SEQ ID 17 and 33

8. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 8 and DNA SEQ ID 18 and 35

9. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 9 and DNA SEQ ID 19 and 37



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 10 and  
DNA SEQ ID 20 and 39

## INTERNATIONAL SEARCH REPORT

International Application No

JP 99/03242

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/705 C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998 see abstract see page 17, last paragraph - page 18, paragraph 1  --- -/--	1-6



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

20 October 1999

Date of mailing of the international search report

18. 02. 2000

Name and mailing address of the ISA

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Authorized officer

Lejeune, R

## INTERNATIONAL SEARCH REPORT

International Application No

/JP 99/03242

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL Accession Number N94214, 19 April 1996 HILLIER L ET AL: "za27c03.r1 Homo sapiens cDNA clone 293764 5' similar to PIR:A54313 androgen-regulated protein FAR-17 - golden hamster" XP002119529 cited in the application 97.8% identity in 357 BP overlap with SEQ ID 11 see page 17, last paragraph - page 18, paragraph 1</p>	1-6
A	<p>---</p> <p>D'ANDREA ET AL: "Molecular Cloning of NKB1. A Natural Killer Cell Receptor for HLA -B Allotypes" JOURNAL OF IMMUNOLOGY, vol. 155, no. 5, 1 September 1995, pages 2306-2310 2310, XP002111500 see abstract paragraph 1 see page 2307, right-hand column, line 16 - paragraph 1</p>	1-6
A	<p>---</p> <p>GILLEN C M ET AL: "Molecular cloning and functional expression of the K-C1 cotransporter from rabbit, rat, and human." JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 271, no. 27, 5 July 1996, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD., US, pages 16237-16244, XP002119528 see abstract paragraph 1</p>	1-6
A	<p>---</p> <p>KYTE J ET AL: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY, vol. 157, no. 1, 5 May 1982, pages 105-132, XP000609692 cited in the application see the whole document paragraph 1</p>	1-6
P,X	<p>---</p> <p>DATABASE EMBL Accession Number AF151861, 1 June 1999 LIN C W: "Homo sapiens CGI-103 protein mRNA, complete cds." XP002119530 99.4% identity in 699 BP overlap with SEQ ID 11 see the whole document paragraph 1</p> <p>---</p> <p>-/--</p>	1-6

## INTERNATIONAL SEARCH REPORT

International Application No

JP 99/03242

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>DATABASE EMBL Accession Number AF153605, 30 June 1999 KIM M K ET AL: "Homo sapiens androgen induced protein (AIG-1) mRNA, complete cds." XP002119531 99.7% identity in 714 BP overlap with SEQ ID NO 11 see the whole document paragraph 1 -----</p>	1-6

### Information on patent family members

/JP 99/03242

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9821328	A	22-05-1998		AU 4885297	A	03-06-1998
				EP 0941320	A	15-09-1999